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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,488	03/25/2008	Brett P. Monia	ISIS.03/PCT-US	7913

25871 7590 09/17/2008
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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
09/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,488	MONIA ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-10,14-20,25,29,31,34,41-43,47-53 and 58* is/are pending in the application.

4a) Of the above claim(s) *1,8-10,14-20,25,29 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34, 41-43, 47-53, and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/7/07, 12/4/06, 7/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence alignment*.

DETAILED ACTION

This Office Action is a response to Applicant's Election filed August 19, 2008.

Claim 34 has been amended.

Claims 1, 8-10, 14-20, 25, 29, 31, 34, 41-43, 47-53, and 58 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group II in the reply filed on August 19, 2008 is acknowledged. Additionally, Applicants election of nucleotides 1194 to 1277 of SEQ ID NO:1 as recited in claim 34 is also acknowledged. The traversal is on the ground(s) that the requirement is improper because the groups identified in the restriction requirement represent different embodiments of a single inventive concept for which a single patent should issue. More specifically, Applicants argue that a single, searchable, unifying aspect links all of the pending claims, that unifying aspect being an antisense compound targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase. This is not found persuasive because while a unifying aspect may link all the pending claims, contrary to Applicant's assertions, a search of these claims would not involve a single search. For example, and as detailed in the previous restriction requirement mailed June 30, 2008, the antisense compounds of the pending claims are considered to be unrelated, since each antisense compound is structurally and functionally independent and distinct because each antisense compound has a unique nucleotide sequence (as per Applicant's disclosure at Tables 1, 15, and 21) and

each antisense compound, upon binding to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, regulates the gene to a different degree (as per Applicant's disclosure at Tables 16 and 28-30). In this regard, the antisense compounds require a different field of search, and therefore, the prior art applicable to one antisense compound would not likely be applicable to another antisense compound, and the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicants next argue that a sufficient search and examination of all the claims can be made without serious burden. Particularly, given the robust and extensive computerized search engines and databases available to the Examiner, Applicants contend that the entire application can be examined on the merits without burden. This is not found persuasive because, as detailed in the previous restriction requirement mailed June 30, 2008, all the inventions listed in the restriction requirement are independent or distinct and there would be a serious search and examination burden if restriction were not required because the inventions have acquired a separate status in the art in view of their different classification; the inventions have acquired a separate status in the art due to their recognized divergent subject matter; the inventions require a different field of search, and therefore, the prior art applicable to one invention would not likely be applicable to another invention, and the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicants also argue that the Patent Office has not shown a lack of unity of invention for the subject matter of the pending claims. Applicants submit that the

reasons leading to the Examiner's conclusion that the disclosed relation does not prevent restriction has not been adequately advanced, and, as a result, the propriety of the restriction has not been established. This is not found persuasive because the previous restriction requirement mailed June 30, 2008 clearly detailed why the disclosed relation between the product and process claims was necessary. For example, the following is paraphrased from the previous restriction requirement mailed June 30, 2008:

> The inventions can be shown to be distinct if the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the antisense compound targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase can be used in a materially different process such as a hybridization probe in a method of identifying p38α mitogen-activated protein kinase gene expression *in situ*, which is a materially different process than the method for decreasing airway hyperresponsiveness or airway inflammation in an animal, comprising administering to said animal, an antisense compound targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase.

However, Applicant is reminded that the Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37

CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Accordingly, claims 1, 8-10, 14-20, 25, 29, and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Additionally, nucleotides 562 to 648 and 659 to 688 of SEQ ID NO:1 and nucleotides 3722 to 3747 of SEQ ID NO:127 as

recited in claim 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 19, 2008.

The requirement is still deemed proper and is therefore made FINAL.

Claims 34, 41-43, 47-53, and 58 and nucleotides 1194 to 1277 of SEQ ID NO:1 as recited in claim 34 have been examined on the merits.

Specification

Applicant's reference to priority in the first sentence of the specification is acknowledged. However, the reference should be updated to reflect applications for patents that are pending.

Drawings

The drawings filed on February 14, 2006 are acknowledged and have been accepted by the Examiner.

Information Disclosure Statement

Applicant's information disclosure statements filed June 7, 2007, December 4, 2006, and June 18, 2006 are acknowledged. The submissions are in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statements, and signed copies are enclosed herewith.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34, 41-43, 47-53, and 58 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of US Patent No. 6,448,079. Although the conflicting claims are not identical, they are not patentably distinct from each other because the antisense compound 8 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said antisense compound inhibits the expression of said nucleic acid molecule p38α mitogen-activated protein kinase and comprises SEQ ID NOs: 90, 91, and 92 claimed in US Patent No. 6,448,079 fully embraces and encompasses the scope of the antisense compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule

encoding a p38α mitogen-activated protein kinase, wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 as instantly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 34, and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,994,076 ('076).

Claim 34 is drawn to an antisense compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1. Claims 41 and 43 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein the antisense compound comprises an oligonucleotide; and wherein the antisense compound is a single-strand or a double-strand compound.

'076 discloses a 26-mer primer with the following sequence:

AAGGGCTTGG GCCGCTGTAA TTCTCT (see SEQ ID NO:1090)

SEQ ID NO:1090 is 100% complementary to at least a 9-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 of Applicant's invention (see attached sequence alignment). Particularly, see nucleotides 1194 to 1203 of SEQ ID NO:1.

Therefore, '076 anticipates claims 34, 41, and 43.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 34, 41, 43, and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,994,076 ('076) in view of Skerra, A. (Nucleic Acids Research, 1992 Vol. 20:3551-3554).

Claim 34 is drawn to an antisense compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase,

wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1. Claims 41, 43, and 47-49 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein the antisense compound comprises an oligonucleotide; and wherein the antisense compound is a single-strand or a double-strand compound; wherein the antisense compound is chemically modified; wherein the antisense compound comprises at least one modified internucleoside linkage; wherein the internucleoside linkage is a phosphorothioate linkage.

Determining the scope and contents of the prior art

'076 teaches a 26-mer primer with the following sequence:

AAGGGCTTGG GCCGCTGTAA TTCTCT (see SEQ ID NO:1090)

SEQ ID NO:1090 is 100% complementary to at least a 9-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 of Applicant's invention (see attached sequence alignment). Particularly, see nucleotides 1194 to 1203 of SEQ ID NO:1.

Ascertaining the differences between the prior art and the claims at issue

'076 does not teach a modified oligonucleotide.

Skerra, A. teaches phosphorothioate-modified primers improve the amplification of DNA sequences by DNA polymerase with proofreading activity (see Abstract). Skerra, A. teaches the introduction of single phosphorothioate bond at the 3' termini of the PCR primer protects the oligodeoxynucleotide from exonucleolytic attack leading to specific and efficient amplification of DNA.

Resolving the level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is considered to be high, being a graduate student or post-doctoral fellow in a biological science.

Considering objective evidence present in the application indicating obviousness or nonobviousness

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an antisense compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 using the teachings and motivation of '076. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the oligonucleotide using the teachings and the motivation of Skerra et al.

One of ordinary skill in the art would have been motivated to make an antisense compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 since '076 teaches that such a compound could be used as an oligonucleotide primer to generate a population of labeled nucleic acids, which is important in identifying differential gene expression. One of ordinary skill in the art would have been motivated to modify the oligonucleotide since Skerra et al. teach the introduction of single phosphorothioate bond at the 3' termini of a primer protects the oligonucleotide from exonucleolytic attack.

There would be a reasonable expectation of success to make an antisense

compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 since '076 taught the successful use and design of such an oligonucleotide to generate a population of labeled nucleic acids. There would be a reasonable expectation of success to modify the oligonucleotide since the prior art taught the successful design and use of modified PCR oligonucleotides (see Skerra et al., for example).

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James "Doug" Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent

Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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> For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

September 13, 2008
/Terra Cotta Gibbs/